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# CLINICAL PROCEEDINGS
## OF THE CHILDREN'S HOSPITAL

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# A Review of the Rubella Problem

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Rubella (German measles) was considered to be a very benign and unimportant disease of childhood until 1941 when Gregg[1] reported the occurrence of congenital cataract associated with maternal rubella early in pregnancy. Gregg's findings were confirmed by Swan and associates[2] in Australia; in the United States identical congenital syndromes following maternal rubella were reported by many writers,[3-9] and in England two cases were reported by Simpson.[10] The relationship between maternal rubella and subsequent congenital malformations in infants therefore has been well established, and the resultant syndrome, known as the "rubella syndrome," includes congenital cataract, deafness, microcephaly, mental retardation and congenital heart diseases. In addition to these, spontaneous abortion, stillbirth, dental defects and other congenital malformations have been attributed to rubella infection during pregnancy. Any of these abnormalities may occur singly as the only congenital defect in a child, or they may occur in various combinations. The cases that have come to light since the first reports appear to differ little from the original syndrome, although other eye abnormalities such as cloudy cornea, glaucoma, buphthalmus, and shallow anterior chamber have been occasionally observed. It remains to be seen whether hypospadias,[2] obliteration of the bile ducts,[11] deformed kidneys,[1] and mongolism[6, 12] which occasionally occur in combination with other components of the rubella syndrome, are incidental findings or part of the condition.

Early reports from Australia state that the risk of congenital malformations subsequent to maternal rubella early in pregnancy is very high, whereas those reports from this country indicate that the incidence is very low. This may be due to the fact that the early investigations were retrospective ones; recent prospective studies have given a more accurate percentage of the risks involved. Since Gregg[1] reported 78 cases of congenital cataract associated with maternal rubella early in pregnancy, many popular magazines and newspapers have introduced the "rubella syndrome" to the public, and a portion of the population has developed a "rubella neurosis." Accordingly, it is the doctor's responsibility, whenever he diagnoses definite rubella early in pregnancy, to inform the patient of the risks involved; it is important to inform the patient of the nature of the possible malformations and the risk percentage to the infant. The physician must

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know how to make an accurate diagnosis of rubella and what the currently accepted means of prophylaxis for this hazard are.

## CLINICAL RUBELLA

According to Wesselhoeft,[13] rubella was first described by two German doctors, De Bergen in 1752 and Orlow in 1758. Thereafter, numerous others called attention to its manifestations, initially assigning it various names but eventually calling it *Roeteln*. Owing to the early interest displayed by German writers, the term *Roeteln* was accepted in England and in the United States; thereafter the disease was known as German measles. Since 1866 the name rubella has been used in English-speaking countries. The early German writers considered rubella to be a modified form of measles or scarlet fever, but we now know that it is an entity unto itself. The terminology of rubella in different countries has been and still is a cause of confusion.

The causative agent of rubella is a filtrable virus. Krugman and Ward[14] found that throat washings from rubella patients could be kept at −40°C. for 10 years and then used to induce rubella. Equally positive results occurred with nasopharyngeal washings in normal saline obtained within 12 to 24 hours after the appearance of the rash from Macaca mulatta monkeys to which the virus was transmitted by intranasal, subcutaneous, intraperitoneal and intravenous routes. Nasopharyngeal washings obtained after the third day of rash were negative.[13]

Anderson[15], in 1948, transmitted experimental rubella by inoculating throat washings in normal saline mixed with penicillin into the respiratory tract. Krugman and associates[16] also demonstrated experimental rubella in 13 patients by inoculating susceptible subjects with material containing acute rubella virus. Two of their patients did not develop a rash; the blood obtained from one of these at the height of his fever was given intravenously to another patient who developed typical rubella with rash 13 days later. Accordingly, Krugman's group proved that rubella can occur without rash during an epidemic.

Distribution of rubella is worldwide, being found in North and South America, Europe, Africa, Asia, Japan, and Australia. Rubella is rare in the first six months of life. Approximately 12 per cent of cases occur among school children; in children's institutions rubella exhibits a fairly high incidence, whereas among day school children the reported rate is low. On the other hand, the rather high incidence of rubella among young adults in colleges and in military life suggests the possibility that more children escape rubella then rubeola. Contagious disease hospitals usually see more cases of rubella among young adults than among children. Rubella appears to be rare in those over 40 years of age. It is conceivable that in the age

group when women are fertile, more females than males contract the disease, as was demonstrated when Hillenbrand[17, 18] observed an outbreak of rubella in a remote community of the Falkland Islands in 1952–1953. Similar findings have been observed by Clayton-Jones.[19]

Naturally occurring rubella usually has an incubation period of between 14 and 21 days with an average of 18 days. However, the experimental rubella of Krugman's group[16] had a five day shorter incubation period than that of naturally occurring rubella.

Rubella is most infective before the appearance of the rash and during the first 48 hours of the eruption; thereafter it is highly probable that infectivity terminates with fading of the rash as in measles.

A lifelong immunity to rubella is usually established by an attack, although late second attacks have been reported. Relapses occur and are not to be confused with late second attacks which are rare. The majority of the so-called recurrent attacks of the disease reflect errors in diagnosis. Some observers noted rubella relapses on the eleventh day, in the third week, in the fourth week, and up to the forty-first day after the original attack. These observers are of the opinion that the establishment of immunity is often delayed, allowing reinfection through subsequent exposure during this period of partial immunity.

Diagnosis of rubella rests on those characteristics that differentiate this malady from the other exanthems, namely the absence of Koplik's spots, the kaleidoscopic character of the rash, the presence of palpable lymph nodes behind the ears and, not infrequently, a pink suffusion of the whites of the eyes in contrast to the sticky mucopurulent conjunctivitis of rubeola. All these features are variable, depending upon the severity of the disease. The manifestations of rubella differ in children and adults. Krugman's group[16] observed naturally acquired rubella involving approximately 250 children and 20 adults. In this series the majority of the children (95 per cent) presented with an illness characterized by normal temperature or low degree fever, three day rash, and posterior auricular and occipital lymphadenopathy. A few patients had a temperature rise as high as 104°F. for 24 hours and an occasional one had no lymphadenopathy. In general, the disease in adults was not so mild. Approximately two days before the onset of the rash adults developed malaise and anorexia, and were conscious of the enlarged and slightly tender lymph nodes. In contrast, the first obvious sign of the disease in children was the appearance of the rash. The lymphadenopathy preceding the rash in children was apparently asymptomatic.

According to textbook descriptions of rubella, the diagnosis does not sound like a difficult one. On a practical level, confirmation of a diagnosis of rubella in the absence of known exposure or during an epidemic is not

easy. There is no pathognomonic sign such as the Koplik's spots found in rubeola (although some have described a "specific enanthem on the soft palate" before the onset of the rash) nor is there any diagnostic laboratory test. Hillenbrand[17, 18] has investigated the blood picture of rubella. He performed white cell counts mostly in the forenoon, stained the blood films by Pappenheim's panoptic method, and did differential counts by Schilling's method, 100 cells being counted. Hillenbrand claims that in clinical and subclinical infections alike, the outstanding feature is the regular occurrence of Turk and plasma cells, which in uncomplicated rubella are invariably present up to the tenth day, and usually persist for many months. The maximum percentages of these cells observed in single specimens were 14 on the third day and 19 on the fourth day. Hillenbrand further says that since blood smears from all cases of rubella (clinical or subclinical) examined between the first and ninth days had plasma cells or Turk's cells which nearly always persisted until the sixth week, a pregnant woman not showing these changes is unlikely to have had rubella and there is no need to fear damage to the offspring or to consider the advisability of therapeutic abortion. This blood picture is substantiated by Ramsay,[20] but most other writers do not agree. Hyperplasia of the postauricular and occipital lymph nodes which typically follows rubella may persist for many months and be accompanied by Turk's cells and plasma cells in the peripheral blood.[17] When persistent lymphadenopathy is associated with these blood changes, a retrospective diagnosis of rubella can be made. Hillenbrand also examined a group of women who became pregnant during an epidemic of rubella. One woman who had had clinical rubella, 2 who had had subclinical infection and 8 who had had no signs or symptoms but had been exposed revealed "the rubella positive blood picture."

Some authorities admit that they cannot often make a diagnosis of rubella when seen in the acute stage of the disease because of its mildness. Accordingly, differential diagnosis of rubella is very important, and includes a long list of infectious diseases and skin eruptions. The rash of *rubeola* is preceded by three to four days of high fever, respiratory symptoms, the development of the pathognomonic Koplik's spots and a mucopurulent conjunctivitis. *Exanthem subitum*, also known as roseola infantum, is a disease of infancy characterized by three to four days of high fever and pharyngitis. It is often associated with a febrile convulsion which is followed by a rash that usually appears as the temperature falls to normal. In contrast, rubella has almost no prodromal stage, and the first obvious sign of the illness is the appearance of the rash. *Scarlet fever* can be differentiated by the characteristic erythematous punctiform eruption associated with an acute exudative tonsillitis or pharyngitis from which group A beta

hemolytic Streptococci may be cultured. Generalized lymphadenopathy, hepatosplenomegaly, a rising titer of the heterophile agglutination test, and atypical lymphocytes in blood smears are indicative of *infectious mononucleosis*. *Drug eruptions* may cause confusion.

In separating rubella from various skin diseases, the typical distribution and duration of the rash (three days), the low grade fever, and the characteristic lymphadenopathy help to establish the diagnosis. The enlarged lymph nodes are not specific for rubella, but may be associated with other infectious diseases and with acute or chronic infections of the scalp or upper respiratory tract. Sizeable numbers of palpable postauricular, occipital and cervical lymph nodes are usually to be found on routine pediatric examinations; some of these are due to heat rash or other types of dermatitis which may then be mistaken for rubella.

## NATURE OF SUBSEQUENT CONGENITAL ANOMALIES ASSOCIATED WITH MATERNAL RUBELLA IN PREGNANCY

### *Failure to thrive*

According to the majority of writers, these babies are of small size, usually present feeding problems, and fail to thrive. The average birth weight of 29 babies with congenital defects was 5 pounds 7 ounces, and that of 13 babies without apparent abnormalities was 6 pounds 10 ounces. Seven babies of the former group, and three babies of the latter were premature. However, even when born at or near term, the congenitally defective babies were sometimes subnormal in weight[2] and many of them came under the care of pediatricians for this complaint before being seen by ophthalmologists or surgeons.[1, 18]

### *Ocular defects*

Congenital cataract: Gregg[1] was the first author to report congenital cataract associated with maternal rubella occurring early in pregnancy. These cataracts are present at birth, are central, nuclear, and subtotal in type; they are bilateral at least three times more often than unilateral. Swan and his associates[2] observed that the opacity of the lens has the appearance of a flattened dense white disk in which six radiating lines are visible. Full mydriasis is difficult, but when it can be obtained, a clear zone is visible peripheral to the opacity. The whole lens is very small. The usual presence of a small cornea, shallow anterior chamber and especially the dense nature of the cataract makes discission difficult. The pupillary reaction to light is weak and sluggish, and in some cases the iris has a somewhat atrophic appearance. An unusually high number of the patients show intolerance to atropine.[1] Of 16 cases of monocular cataract, 10 had microphthalmia. Nystagmus and buphthalmos occur

infrequently.[2] Rones[9] studied 4 cases of ocular defects; in the infants of two mothers in whom the exanthem occurred during the second month of pregnancy, cataract developed, whereas in two mothers in whom the disturbance occurred during the third month of pregnancy, congenital glaucoma appeared in the offspring. Similar findings have been reported by other authors.[3-5, 7, 10]

Retinopathy: Peculiar pigmentary changes in the fundus have been described by many observers. This condition may be seen most clearly in cases of deafmutism without cataracts, or in the unaffected eye in some cases of unilateral cataract. The discrete lesions have a "measly or blotchy appearance" involving the macular region and an area of three to four disc diameters surrounding it. In some cases distribution is much wider and appears on the nasal side of the disc. In a few cases there is a deficiency of pigment in the area adjacent to the disc, but this condition has no harmful effect on vision.[21] The embryologically "critical period" for the eyes is from the fourth to the tenth week of pregnancy; the average is six weeks.

*Cardiac defects*

A congenital cardiac defect was present in a large proportion of Gregg's series;[1] this was always of the acyanotic type. Of Gregg's 78 patients with congenital cataracts, 44 had congenital heart disease. Patent ductus arteriosus was the most frequent defect and was present in every case in which the baby was small and ill nourished and in which there were feeding difficulties. In cases without a congenital cardiac defect, the physical development was noticeably better.

Stuckey,[22] in Australia, examined 426 cases of congenital heart disease during a period of five years and found 44 in which the patients had a history of maternal rubella during pregnancy. Twenty-seven of these (aged 3 months to 12 years) were referred to the congenital heart disease clinic as part of a special survey of rubella. Of the 27 patients, 13 had patent ductus arteriosus, 4 had ventricular septal defect, 3 atrial septal defect, 2 tetralogy of Fallot, and 1 each, aortic stenosis, pulmonary stenosis, coarctation of the aorta, Eisenmenger's complex and transposition of the great vessels. Patent ductus arteriosus occurred about eight times more frequently than other forms of congenital heart disease compared with the normal relative incidence in the general population. Female preponderance was 11 to 2 in those with a patent ductus arteriosus. Of the above 27 patients with congenital heart disease following maternal rubella, 10 of the 13 with patent ductus arteriosus and 6 with other congenital heart defects were born in 1940 during an epidemic of rubella. Stuckey calculated the incidence to be 28 per 1,000 live births with patent ductus arteriosus and

17 per 1,000 with other congenital heart lesions. He quoted the normal incidence of congenital heart disease in the general population aged 3 months to 15 years as 1.8 per 1,000 and of patent ductus arteriosus as 0.3 per 1,000. Thus, the incidence of patent ductus arteriosus in children born of mothers who had suffered from rubella during pregnancy in that epidemic was about 88 times the expected incidence, and the incidence of other congenital heart lesions about 11 times the expected incidence. His explanation for the increased incidence of patent ductus arteriosus was as follows: The cardiac septa, and the main vessels and their valves are only susceptible to damage by environmental factors for a period of four or five weeks during fetal life. The ductus arteriosus, on the other hand, is present for many months of fetal life and for a short time after birth, and whatever the mechanism of final closure it is conceivable that it could be damaged at any time. Stuckey added, "the greater incidence of patent ductus arteriosus in these children may thus merely reflect the longer time that this structure is at risk." If this explanation is accepted, the fact that patent ductus arteriosus does not predominate unduly over other congenital cardiac defects in the general population may suggest that genetic rather than environmental factors are responsible for the great bulk of cases of congenital heart diseases. The presence of some other factor, possibly genetic, is suggested by the fact that there is a strong female preponderance in all cases—including those thought to be related to rubella.

According to a study from Massachusetts by Rustein and his associates,[23] birth dates of all children born with congenital heart disease have a seasonal pattern which differs from that of all live births, being more frequent than expected in the months of April and May and in the months October through January. This seasonal distribution of all cases with congenital heart disease might be the result of a similar seasonal pattern in one or another of the constituent specific anomalies. In addition, they noted an increased frequency of winter birth dates for children with patent ductus arteriosus.

Rustein and associates[23] have also pointed out that the distribution of birth dates of children with patent ductus arteriosus in all months of the year with a higher incidence in the late autumn and early winter suggests that two types of etiologies might exist. The first would include the majority of cases, probably due to many nonspecific causes; the second, represented by the "excess" of cases in October through January, apparently is responsive to a seasonal factor, probably rubella.

Infection with the rubella virus may affect the anatomical design of the mechanism which closes or obliterates the ductus after birth. Swan,[11] in examining the patent ductus arteriosus of three infants at post mortem, found that these differed structurally from the normal ductus arteriosus.

The internal elastic lamina was absent or ill defined, the lumen was larger, the walls were thinner, and there was some replacement of muscle by collagen fibers. Further study including normal controls, however, is needed to confirm this point.

*Deafness*

Deafness in infants whose mothers had rubella during pregnancy was first described when Swan's group[2], in 1943, reported a series of 49 infants, of whom 7 had deafmutism (5 females, 2 males). In general, these patients were not totally deaf, but could still hear high-pitched sounds such as train whistles. When speech was present, it was limited to a few words such as "Mum" or "Dad." In no case was there any evidence of hereditary deafmutism. The age of the patients prevented the assessment of bone-conduction and air-conduction, but the impression was that bone-conduction was better than air-conduction for high tones. Low tones did not seem to be appreciated.

Clayton-Jones[19] found 11 out of 123 children in institutions for deaf children in England with a positive history of maternal rubella during pregnancy. These 11, who were born during the late fall and winter, had bilateral incomplete inner ear deafness, usually fairly uniform throughout the frequency range; Carruthers' study[24] gave similar results, but on the basis of caloric stimulation of the labyrinth, he felt that the semicircular canals are largely spared in these cases, the main damage being to the cochlea. In one of his patients (with congenital cataract and a patent ductus arteriosus) who died at 6½ months of age, the outstanding feature of the inner ear at necropsy was the total absence of any differentiation of primitive cells to form the organ of Corti in the cochlea. The eighth cranial nerve and spiral ganglia were formed, as were the bony and membranous semicircular canals, although the receptor and end organs showed the same lack of cell differentiation as the organ of Corti. The average duration of pregnancy of the mothers of these children at the time of onset of the exanthem was 2.1 months.

Aycock and Ingalls[25] feel the "critical period" for ears is the first nine weeks of pregnancy. Clayton-Jones[19] has pointed out that these children with deafmutism whose mothers had rubella during the first three months of pregnancy usually had partial hearing, since the cochlea is partly formed by the time of this "critical period" for ears. The tympanic cavity separates in the ninth week, and the drum and final stages of the meatus and external ear form later. The fact that these escape damage must depend on factors other than those of development, since otherwise one would expect malformations of the middle and external ear in children born to mothers who

had rubella in the third or fourth month of pregnancy. Clayton-Jones suggests a local tissue susceptibility as a typical feature of rubella infection. Lindsay and Harrison[26] have described the pathology of rubella deafness and commented that rubella in the first trimester of pregnancy produces the Schiebe's type or sacculocochlear type of malformation of the inner ear in the child. This they explained as follows: The lesions are presumably produced by a blood-borne toxin or virus and the stria vascularis has the best blood supply of all the structures in the membranous labyrinth. The endolymph of the affected areas might contain a higher concentration of the irritant and this could explain a predilection for damage to saccule and cochlea. It is also possible that the utriculoendolymphatic valve effectively isolates the utricle and semicircular canals from the cochlear portion of the labyrinth. Possible confirmation to this theory is the extensive atrophy of the stria vascularis present in patients with Meniere's disease who had good hearing.

The incidence of deafness in the rubella syndrome varies according to the writer from 20 to 72 per cent.[2, 11, 24, 27-29]

*Mental retardation and microcephaly*

Many authors[6, 30, 31] have observed mental retardation and microcephaly associated with the rubella syndrome, particularly when there is more than one of the other three main defects: cataract, deafmutism, and the heart abnormalities. Gregg[21] believes that in some there is a condition of mental retardation, *per se*, which is not merely the result of defects of the organs of special sense. Many of the affected children present a truly pathetic sight, amounting at times to complete imbecility. He noted that they exhibited an extreme degree of head-banging, and also a considerable incidence of Francesschetti's sign, digito-oculare, where they appeared to be trying to gouge out their eyes. Gregg also pointed out that "they are frequently overbright." They are always on the move, are lacking in any sustained concentration, and are a source of great worry and anxiety to their mothers. Many authorities claim that if these children are taken in hand early enough, and provided also that the parents are themselves trained in the correct principles of management, the standard of intelligence for this group of children can be raised considerably. However, Gregg feels that some have mental retardation of such a degree as to be beyond any real rehabilitation.

Undoubtedly, microcephaly is found in these children. In Albaugh's series[3] of 9 cases of congenital abnormalities in the infant following rubella in the mother in the first trimester of pregnancy, there were 5 cases of microcephaly. However, an over-all incidence is not known.

*Dental defects*

Evans[32] found that of 34 babies whose mothers suffered from rubella during pregnancy 23 exhibited congenital dental anomalies; in 18 the anomalies were major ones such as "sharklike" and pointed incisors and enamel hypoplasias. All except 2 of these infants showed other congenital malformations. Dental defects are most marked in the infants whose mothers had suffered from rubella between six and nine weeks of pregnancy, considered to be the "critical period" for dental development.[25, 32] The main dental abnormalities consisted of retardation of eruption, enamel hypoplasia, and dental caries.

*Stillbirth and abortion*

The intensity of the abnormalities associated with the rubella syndrome is variable, ranging from dental defects to spontaneous abortion or stillbirth. According to Budolfsen,[31] the incidence of abortion or stillbirth associated with the rubella syndrome is estimated as 10 to 20 per cent. Lande[30] states that maternal rubella occurring after the termination of organogenesis in the fourth fetal month does not produce germinal damage; he believes it may, however, cause stillbirth. Swan[33] investigated the records of 760 cases of stillbirth in South Australia in the period 1939 through 1945. Of 16 cases of maternal rubella (1 case was doubtful) during pregnancy, 13 took place during the first four months. He concluded that rubella was the only disease which showed this high incidence in the early months and he suggested that rubella may be a factor in the causation of stillbirth by damaging the embryo early in pregnancy.

ETIOLOGY OF RUBELLA SYNDROME

Nothing is known of the mode of action of the rubella virus. Possibly the virus invades the cells which are about to divide and differentiate rapidly, thus inhibiting their normal development. It is possible also that the virus may affect chiefly the embryonic vascular system, injuring the heart directly and other tissues such as the organ of Corti indirectly by damaging their nutrient vessels.[24] In an attempt to explain the production of malformations by the rubella virus acting early in fetal life, it has been assumed that only cells which are in active division are affected, while fully formed organs and quiescent primordia tend to escape. In this view, there is a critical period in the development of each organ during which it is susceptible to attack. The virtual confinement of congenital defects to infants whose mothers suffered from rubella during the first three months of pregnancy suggests that it is only during this period that the embryonic cells are highly susceptible to the etiological agent of rubella. The experience that undifferentiated embryonic tissue is especially susceptible to

viral infection has long been well known and used in the laboratory; for example, viruses are grown on chick embryo for experimental and therapeutic purposes. On first consideration, it might seem logical to assume that since the virus of rubella appears to attack the ectodermal structures in the adult it might do likewise in the embryo. Another possibility which may be considered is that after the formation of the placenta at the end of the third month of pregnancy, the barriers between mother and fetus become less penetrable to the causative factor of rubella. As far as this explanation is concerned, it may be mentioned that there is evidence that even late in pregnancy, other viruses, for example those of smallpox and measles, are still capable of penetrating the placental barrier. The actual mechanism of production of the congenital defects described has yet to be determined.

It has been established that other viral infections occurring during the first three months of gestation may cause characteristic congenital malformations in the human fetus. Swan[11] postulated that severe viral infections such as measles or influenza may kill the fetus and lead to spontaneous abortion, whereas the milder viral diseases such as rubella may cause only damage to the fetus. From the fourth fetal month, after the termination of organogenesis, rubella does not produce germinal damage to the fetus, though it may, however, probably still cause stillbirths or congenital anomalies.

Warkany and Schraffenberger[34] induced multiple congenital malformations in rats both with a riboflavin-deficient diet and a vitamin A-deficient diet. Congenital malformations have been experimentally induced in the skeleton of rats by maternal riboflavin deficiency. Shortening of the mandible, radius, ulna, tibia and fibula, various forms of syndactylism, and cleft palate were observed in the affected young. These authors also induced multiple congenital malformations in soft tissue organs in rats, the mothers of which were reared and bred on a vitamin A-deficient diet. In the newborn of such mothers congenital anomalies of the eyes have been observed; the most frequent ocular anomaly was a retrolenticular membrane which occupied the normal location of the vitreous body; folding and coloboma of the iris and ciliary body, and "open eye" were also noted. The ocular anomalies were usually symmetrical and almost identical in all members of a litter. Gillman's group[35] induced congenital malformations by the injection of 1.0 cc. of trypan blue into female rats before conception and during pregnancy. They found a high incidence of such congenital malformations as hydrocephalus, spina bifida, and eye defects, and a lesser incidence of tail defects, meningocele, harelip, cleft palate, ear defects, imperforate anus, clubfoot and dislocation of the fore and hind limbs. They suggested that in the absence of positive information relating to the

passage of the virus of rubella through the placenta, rubella and other mild infections probably produced their effects on the human embryo in a manner similar to that described for trypan blue in the rats.

Fox and his associates[36] examined all reports of measles, mumps and chickenpox sent to the Milwaukee Health Department in the period 1942 through 1945, and then interviewed married women with these infections to determine the incidence of congenital anomalies among their offspring. They compared their findings with those of other authors and noted the incidence of anomalies related to different viral diseases during pregnancy. Of 665 children born of mothers whose pregnancies were not complicated by any of these viral infections, 0.9 per cent had congenital anomalies. Of 33 live children born to the same number of married women who had had measles, mumps, or chickenpox while pregnant, one had a congenital anomaly. One pregnancy ended in a spontaneous abortion in the second month. None of 22 children born of pregnancies complicated by mumps and none of 4 children born of pregnancies complicated by chickenpox showed congenital defects. One of 7 children born to a pregnancy complicated by measles had a unilateral harelip. The authors found that anomalies followed maternal rubella during pregnancy at about 15 times the expected rate of 0.9 per cent, and in those mothers who had had rubella in the first four months of gestation, the rate was more than 18 times that expected (table 1).

### THE RISK INVOLVED

The risk of congenital malformations resulting from maternal rubella infection acquired during the first trimester of pregnancy has been vari-

TABLE 1

*Anomalies Following Maternal Virus Diseases by Period of Pregnancy (Adapted from Fox[36])*

| Disease | Source of Data | Period of Pregnancy | No. of Children | No. with Anomalies |
|---|---|---|---|---|
| Rubella | Fox and Bortin (1946)[37] | 1st 4 months | 9 | 1 |
| | | 5 mos. and after | 2 | 0 |
| Rubella | Aycock and Ingalls (1946)[25] | 1st 4 months | 3 | 1 |
| | | 5 mos. and after | 1 | 1 |
| Poliomyelitis | Ibid. | 1st 4 months | 24 | 2 |
| | | 5 mos. and after | 74 | 0 |
| Measles | Fox, et al. (1948)[36] | 1st 4 months | 2 | 1 |
| | | 5 mos. and after | 5 | 0 |
| Mumps | Ibid. | 1st 4 months | 10 | 0 |
| | | 5 mos. and after | 12 | 0 |
| Chickenpox | Ibid. | 1st 4 months | 2 | 0 |
| | | 5 mos. and after | 2 | 0 |
| None | Ibid | | 665 | 6 |

ously estimated to be from 10 to 90 per cent. Many of the earlier data were accumulated by the retrospective method; questionnaires were sent to the mothers or the physicians concerned. This type of investigation can, however, be very misleading, and in recent years, several prospective surveys have been done. Miller and colleagues[38] state that the uncertainty of diagnosis of rubella, the mildness of the infection and its ubiquity, as well as the inability to determine accurately the onset of pregnancy will continue to hamper the collection of accurate statistics dealing with this relationship. The percentage risk of congenital abnormalities associated with maternal rubella is high in the Australian reports (Gregg[1], the Swan group[2]) and very low in the American reports (Fox and Bortin,[37] Miller[38]). Lundström,[39] in a retrospective study of the rubella epidemic in Sweden in 1951, found that rubella during the first four months of pregnancy had a demonstrable effect in the form of stillbirth, neonatal death, anatomically demonstrable abnormalities, and prematurity. The total incidence was approximately 17 per cent as compared with 6 per cent in the concurrent control series. Brown and Nathan,[40] in a similar study in Manchester, England, found congenital anomalies in 17.9 per cent of children whose mothers had rubella during pregnancy; their concurrent control study revealed an incidence of 2 per cent.

Prospective studies in which the case is selected before the child is born are likely to provide more accurate figures. Hill and Galloway[41] investigated National Health Insurance records in England, and found the incidence of congenital malformations associated with maternal rubella was 20 per cent if the disease was contracted during the first trimester of pregnancy, and no incidence if contracted during the second and third trimesters of pregnancy. They also added that 6 cases of rubeola which occurred in the first, fourth, fifth, seventh, and ninth months of pregnancy revealed no abnormalities in the offspring, and one case of varicella contracted in the fifth month of pregnancy also resulted in a normal baby. Ingalls and Purshottam[42] conducted a prospective study concerning the risk of congenital malformations associated with maternal rubella, and found an incidence of 8 per cent if the disease was contracted during the first trimester of pregnancy, 20 per cent if contracted during the second trimester of pregnancy, and none if contracted during the third trimester of pregnancy. It is noteworthy that the incidence of risk found by Hill and Galloway[41] (prospective study) and the incidence noted by Lundström,[39] and Brown and Nathan[40] (both retrospective studies), are nearly the same. Ramsay[20] has pointed out the significance of the prospective study, and in quoting Ingalls and Purshottam's figure of 17 per cent for deformity and stillbirth resulting from the rubella infection in the first three months of pregnancy, states that the risk of 1 in 5 is grave enough to warrant a very careful assessment in any individual case and the use of such prophylactic measures as are

available, even though it is now believed the risk of fetal damage from rubella even at the eighth week of pregnancy is not so high as the original figures suggested.

### PROPHYLAXIS OF THE RUBELLA SYNDROME

Since Gregg's original report, many articles in popular magazines and newspapers have induced the "rubella neurosis." Accordingly, even the layman seems to know a great deal of the risks involved. Actually, the exact risk involved in terms of the percentage of such pregnancies which end in the birth of a defective child is not known. However, based on the reported evidence, there is no doubt that a relationship exists between the appearance of rubella in the mother early in pregnancy and the subsequent appearance of certain congenital abnormalities in the offspring. This association has appeared so striking to some authors that they have advised therapeutic abortion in instances where pregnant women have acquired the disease early in pregnancy. Others have urged that young girls be exposed deliberately to the disease early in life for the purpose of acquiring lasting immunity. Finally, many have suggested that exposed pregnant women be passively immunized with convalescent serum or immune serum globulin.

Anderson[15] has induced experimental rubella in human volunteers by inoculating throat washings from a patient with rubella. He states that there is strong circumstantial evidence that this artificially induced rubella will protect the individual with a high degree of subsequent immunity in the presence of a rubella epidemic for at least six to nine years; accordingly an artificially induced rubella infection in a woman of 20 could be expected to insure virtually complete immunity over the usual child-bearing period in a modern community. Anderson also stressed that this type of immunization program would call for strict isolation of the subject during the period of her infectivity, for example in a "holiday camp." This idea was initiated by Wesselhoeft[13] and has received support from many authorities. Schick[42], however, in making an analogous observation from smallpox, considered that some women who had already had rubella might pass the virus via the placental circulation to the fetus without themselves suffering from a clinical attack of the disease. He postulated that in such cases the immunity is a cellular one which allows the circulation and multiplication of the virus until antibodies are mobilized; this clearly could not happen if the immunity were humoral. This idea has also received some support from Lundström.[39]

Gregg[21] first mentioned the convalescent rubella serum service in Australia; the New South Wales Red Cross Blood Transfusion Service has made convalescent serum available to the medical profession since 1949

TABLE 2

*Incidence of Rubella in Pregnant Women Exposed to Rubella Who Received Injections of Convalescent Sera as Compared to a Control Group (Gregg[21])*

| Classification | Treated | Control |
|---|---|---|
| Exposed | 456 | 148 |
| Contracted rubella | 5 | 17 |
| Did not contract rubella | 451 | 131 |
| Incidence | 1.1% | 11.5% |

for administration to women exposed to rubella in the first 16 weeks of pregnancy. The serum is obtained from volunteers approximately three weeks after the disappearance of the rubella rash, and is not pooled. Thirty milliliters of this serum is injected intravenously within five days of exposure. Gregg's results suggest that this procedure may be worthwhile (table 2), but one must not forget that normal adult and convalescent serum both carry the risk of homologous serum jaundice. Gamma globulin seems to be free from this risk, the dose is small, and the occasional reactions it produces are rarely severe. Gamma globulin, preferably prepared from convalescent serum, therefore seems the most promising immunizing agent, although its true efficacy in rubella is still to be determined.

In England, the Ministry of Health[44, 45] recommends that 750 mg. of gamma globulin be given to any woman in the first four months of pregnancy as soon after exposure to rubella as possible. It also comments that gamma globulin is useless after symptoms of the disease have developed, and that gamma globulin prepared from convalescent rubella serum, if available, would doubtless be a more potent prophylactic measure. It is also stressed that no attempt should be made to protect young girls after exposure to rubella, since a natural attack of the disease confers far greater immunity than gamma globulin and carries a complication rate of only 1 in 6,000. Landon's group[46] suggested that gamma globulin, in a dosage of 0.1 ml. per pound of body weight administered on the day of supposed exposure, is protective against rubella for somewhat less than 19 days. In their series, despite the intimacy of contacts in an institutional epidemic, the attack rate was low (17 per cent in the control group), and it was noted that the older the child, the greater the tendency to escape the disease in either injected or control group.

Korns[47] investigated the prophylaxis of rubella with three separate lots of gamma globulin in doses of 0.1 ml. per pound of body weight. Protection appeared to be afforded by one of the lots of gamma globulin, but the other two lots failed to show significant evidence of protection. For the prevention of German measles in the exposed pregnant woman, it seems

essential that a known product be utilized, possibly immune serum globulin made from convalescent German measles serum. In the absence of such material there may still be merit in using the ordinary immune serum globulin for such protection.

Anderson and McLorinan,[48] on the basis of three controlled series, concluded that although the most probable interpretation of a controlled trial in an epidemic is that one person in every two given gamma globulin is protected against rubella, figures for the control group and the gamma globulin-treated group did not differ to a statistically significant degree.

Very recently, Krugman and Ward[14] have demonstrated neutralizing antibody present in both ordinary and rubella-convalescent gamma globulin as well as convalescent-phase plasma. Serum drawn on the first day of rash from patients with rubella was mixed with normal human serum, gamma globulin, convalescent-phase plasma, and convalescent-phase gamma globulin respectively, and each mixture was injected intramuscularly into the test subjects. On the basis of the results shown in table 3, these authors have recommended that pregnant women exposed to rubella in the first trimester of pregnancy be treated as follows: All women with no previous history of rubella who are in the first trimester of pregnancy should be given at least 20 ml. of gamma globulin intramuscularly as soon after exposure as possible; if convalescent-phase gamma globulin is available they recommend 10 ml. as an adequate dose.

The above investigations have shown that although ordinary gamma globulin and convalescent rubella gamma globulin will sometimes prevent rubella, neither has proved consistently effective. By modifying rather than completely preventing rubella, these agents carry the risk of a "masked

TABLE 3

*Demonstration of Rubella Neutralizing Antibody in Gamma Globulin and Convalescent-Phase Plasma (Krugman and Ward[14])*

| Material Administered* | Number of Subjects | Number Contracting Rubella | Incubation Period |
|---|---|---|---|
| | | | *days* |
| Rubella serum plus normal serum (no antibody) | 6 | 5 | 15, 15, 15, 17, 17 |
| Rubella serum plus gamma globulin | 6 | 1 | 17 |
| Rubella serum plus convalescent-phase plasma | 6 | 1 | 14 |
| Rubella serum plus convalescent-phase gamma globulin | 6 | 0 | |

* Equal volumes of rubella serum and material to be tested mixed and administered in dose of 1.0 ml. intramuscularly.

attack" of rubella without a rash, and the patient may proceed to term unaware that the fetus may have been affected. The use of gamma globulin may therefore give one a false sense of security.

Some authorities have advised therapeutic abortion in instances where pregnant women have acquired rubella early in pregnancy. Wesselhoeft[49] has pointed out that there are insufficient data at hand to warrant therapeutic abortion in these mothers. Hecht[50] from Denmark, reported 10 pregnant women between 16 and 33 years of age who underwent prophylactic abortion in the period 1954–1955 because of maternal rubella; 9 of the 10 fetuses were deformed.

Ramsay[20] stresses that therapeutic abortion need never be undertaken as a panic measure, and certainly after the fourth month of pregnancy contact with a case of rubella need cause no anxiety. He suggests that if there is contact with a proven case of rubella before the fourth month of pregnancy, the pregnant mother should be given gamma globulin in an intramuscular dose of 750 mg. White blood counts should then be done on alternate days between the fourteenth and twenty-fourth day after contact. The appearance of Turk cells and plasma cells in the peripheral blood in conjunction with lymph node enlargement, even in the absence of a rash, strongly suggests a subclinical attack. In such cases, Ramsay believes that the question of a therapeutic abortion should be considered. The situation should be carefully explained to both husband and wife and discussed in the light of their wishes and religious conviction.

Krugman and co-workers[16] have emphasized the necessity of individualizing each case and agree with other authorities that there is in any event ample evidence to indicate that the risk to the fetus is significant enough to warrant the recommendation of therapeutic abortion under certain circumstances. Their solution is interesting and quite logical; they stress that the management of the rubella problem must be individualized in every case, and all factors must be weighed carefully by both doctor and patient. In the case of a young, healthy, recently married couple whose child-bearing future is bright, the decision to give gamma globulin would depend on whether or not the consent to therapeutic abortion is obtained in the event rubella develops. If there were no legal, moral, ethical, or emotional contraindication to abortion, they would advise that gamma globulin be withheld in order not to mask the disease. If, on the other hand, the couple felt that they would not wish an abortion under any circumstances, gamma globulin is advised. In either case, if rubella did not occur, the pregnancy would be allowed to go to term. If the patient developed rubella, it would be the responsibility of the physician consulted to inform the couple of the risk involved. The final decision should be made by the prospective parents. An elderly couple, childless for 15 years, in all probability would want to

take the risk; consequently, gamma globulin would be given and no abortion would be considered even if rubella developed.

At the present time, the most effective method of attacking the rubella problem is to encourage deliberate exposure to this disease before the childbearing period. This active immunization procedure carries with it the danger of increasing the spread of rubella in the community. Consequently, it must be rigidly controlled in an attempt to eliminate this hazard to the pregnant woman. In this respect Wesselhoeft's "measles camp"[13] and Anderson's "holiday camp"[15] seem to be the best solution.

SUMMARY

Rubella (German measles) was believed to be a benign disease of childhood until 1941 when a definite relationship was found between congenital cataracts in the fetus and maternal rubella during the first trimester of pregnancy. Since then, this syndrome has become known as the "rubella syndrome," which includes congenital cataracts, deafness, mental retardation, microcephaly, and congenital heart disease. In addition, spontaneous abortion, stillbirth, dental defects, and other congenital abnormalities in the fetus are attributed to maternal rubella occurring during pregnancy. The three major defects are congenital cataracts which are frequently bilateral, subtotal, central and nuclear in type, deafness which is of a sacculocochlear type of the inner ear, and congenital heart disease, most frequently patent ductus arteriosus.

The embryologically critical period for the eyes is the fourth to tenth week of pregnancy, for the heart, the first four or five weeks of fetal life, and for the ears the first nine weeks of pregnancy.

The practical difficulty of diagnosing rubella is due to the absence of a pathognomonic sign such as the Koplik's spots seen in rubeola, although the kaleiodoscopic nature of the rash, the pink suffusion of the whites of the eyes, and the postauricular and occipital lymphadenopathy are helpful.

The risk of congenital defects in the fetus resulting from maternal rubella infection acquired during the first trimester of pregnancy has variously been estimated to be from 10 to 90 per cent by retrospective and prospective methods. Much of the earlier information was accumulated by retrospective methods which revealed the highest percentage, and is likely misleading. The recent prospective methods reveal an incidence between 10 and 20 per cent which is probably more accurate but still serious enough to warrant a question of interruption of the pregnancy.

To prevent these hazards of the rubella syndrome in the fetus, many trials with gamma globulin, convalescent serum, and convalescent gamma globulin have been carried out without any definite promise. A further study is warranted.

A deliberate exposure to rubella before the child-bearing age, at which time the disease offers a lasting immunity, seems to be the best means of prophylaxis of the rubella syndrome at present.

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# Foreign Bodies of the Nose and Ears of Children

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Any doctor spending much time in a pediatric hospital emergency room will see all types of foreign bodies in the noses and ears of children brought in by their excited parents. At first the object or foreign body is situated well forward in the nose or externally in the ear canal. Unskillful attempts at removal by the patient or others often push it further back. Because symptoms and technique of removal differ, foreign bodies in the nose and ears will be discussed individually.

## FOREIGN BODIES IN THE NOSE

Anything small enough to pass through the external nares may be found lodged in the nose. Examples include stones, beads, seeds, and buttons. If a foreign body remains in the nose a long time under conditions of filth and poor hygiene, maggots and worms may be found. Foreign bodies may also lodge in the nose by way of the nasopharynx from vomiting or coughing when swallowing. Occasionally a small, almost minute, foreign body may become the nucleus for a crystalline concretion called a rhinolith.

Frequently the parent will see the child put the foreign body in the nose or notice an object in the nasal orifice. The early symptoms of pain, sneezing from local irritation, or unilateral nasal obstruction often indicate the

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presence of a foreign body. However, in some cases there may be no early symptoms. This is especially true if the foreign body is small, smooth, and hard and not prone to swelling.

Absence of symptoms may prevent discovery of the foreign body for weeks or months. A secondary infection develops in the nose and pain occurs due to congestion and swelling of the nasal mucosa. Pressure necrosis may involve the cartilage, and ulceration and granulation tissue formations may lead to nasal hemorrhage; sinusitis may develop, and cases of generalized cellulitis have been described. Symptoms of late discovery of a foreign body include bleeding from the nose, and one-sided nasal blockage with foul discharge and/or breath odor. Any child with breath odor or unilateral foul nasal discharge should be considered to have a foreign body in the nose.

The patient's nose should be examined carefully with a nasal speculum and, if possible, by an indirect mirror examination of the nasopharynx. Thorough examination of the nose and removal of the foreign body may be facilitated by the use of a nasal shrinking agent such as phenylephrine or epinephrine topically. Treatment, however, depends on 1) cooperativeness of the child, 2) location of the foreign body, 3) the nature and size of the material, and 4) the length of time the foreign body has been present.

Several different methods of removal may be used:

1) If the child is co-operative he may be told to hold the unobstructed nostril and blow forcibly out the nostril containing the foreign body. This method is safe and can save unnecessary instrumentation when it is successful in removing the foreign body.

2) The most successful removal of foreign bodies is accomplished by the use of a curved probe such as a Eustachian catheter or a curved ear curette. The method is to place the curved probe behind the foreign body, usually over the top of it, and then pull forward. It is desirable to use a shrinking agent and local pontocaine or cocaine before removal to lessen pain and open the nasal air space. These medications are also useful in finding posteriorly located foreign bodies present for a long period of time. If the child is unco-operative, he should be restrained and held as still as possible, and the curved probe method described above attempted.

3) Grasping forceps can be used but with the danger, especially in an uncooperative child, of pushing the foreign body farther posterior. These cannot be used on a large object or one of very soft material.

4) The nose may be irrigated with normal saline. The opposite nostril is always irrigated to wash the foreign body forward rather than backward. Care must be taken not to push the foreign body back into the nasopharynx when removing it because of the danger of aspirating it into the trachea.

Since the nose has many hidden corners and crevices it is sometimes

impossible to see the postero-superior area. X-rays can assure complete removal when the object concerned is radio-opaque.

In some uncooperative children with large impacted foreign bodies it is best to perform the removal under general anesthesia.

### FOREIGN BODIES IN THE EAR

As with the nose, any foreign body small enough to pass into the external ear opening may be found lodged in the canal. Foreign bodies may be present for a long period of time without symptoms, depending on their size, site in the canal, and character. Symptoms will include deafness, a sense of fullness or stopped-up ear, itching, and tinnitus. Pain and discomfort occur when the object is deeply lodged or pointed and sharp-edged in character.

Foreign bodies of the ear may be classified into:

1) Animate or living, as roaches, beetles, and other insects.
2) Inanimate, as beads, stones, seeds, and buttons.
3) Hygroscopic (absorbs water and swells), as beans and other vegetable matter.
4) Cerumen or wax.

1) Animate foreign bodies of the ear are usually associated with a lack of personal hygiene. Regardless of occurrence, the patient is greatly alarmed due to the fluttering of the wings and feet touching the acutely sensitive drum membrane. Alcohol instilled in the ear kills the insect. The insect can then be readily irrigated from the ear with warm water or saline and a metal syringe. There are two important points to remember when irrigating an ear: a) Point the tip of the metal syringe at the posterior canal wall rather than directly at the drum or foreign body. This will wash out the body more easily and there is less danger of injuring the tympanic membrane and middle ear if the patient moves; b) always use water at body temperature or slightly warmer. Ideally a temperature of 105°F. is best. If cold or hot water is used, stimulation of the labyrinthine mechanism will cause the patient to become dizzy and even to vomit.

2) Inanimate foreign bodies *per se* in the ear canal are not harmful and may be present for a long time without any symptoms. They are, however, harmful when unskilled attempts are made to remove them. Abrasions of the ear canal, ruptured drum membrane, and even middle ear damage can be caused. Included in this group of foreign bodies are otoliths which are concretions formed in the auditory canal and associated with chronic suppurative otitis media.

The location of foreign bodies in the canal may be superficial or deep; they may even touch the drum membrane. Superficial foreign bodies may be removed with a ring curette if they are not wedged too tightly. However, if the child is not co-operative and perfectly still, instrumentation should not be used. Forceps or hooked prongs do not work well and usually cause the body to be pushed in more deeply. In uncooperative children and in all cases where the foreign body is located deep in the ear canal, irrigation with a metal syringe as previously described is the best method of removal.

Repeated attempts at removal of a foreign body can traumatize the ear and be very painful to the child. Removal under general anesthesia may be more successful to facilitate removal than repeated attempts without anesthesia in an uncooperative patient.

3) Hygroscopic foreign bodies, for example, beans, absorb water and swell. Alcohol and oily solutions are best for irrigating them out of the ear canal. When these are not available, saline irrigation may be used.

4) Cerumen is the most common foreign body encountered in the ear. It differs from other foreign bodies since it is not a medical emergency. Some children with oily skin and active wax-secreting glands in the ear canal accumulate enough cerumen to block the external ear. Two types of cerumen are encountered: a) soft and oily, and b) hard and dry. The soft, oily type is no problem since it comes out readily with a curette or irrigation with a metal syringe. The hard, dry type should not be removed with curettes or cotton tips in unco-operative children. Curettes may traumatize the ear canal, and cotton tips push the cerumen deeper in the canal. Various types of ear drops such as sodium bicarbonate, oils, alcohol, and peroxide have been used but are not very successful. A recent product, Cerumenex®,* dissolves and liquefies hard cerumen. It can be used in two ways: 1) Fill the ear canal with it and hold it in the ear for 15 to 20 minutes. Then irrigate the ear. 2) Prescribe Cerumenex (3 drops three times a day) and have the patient return in three days to have the ear irrigated.

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* Cerpan (triethanolamine polypeptide oleate-condensate) 10% in propylene glycol with chlorbutanol 0.5%.

# Lymphangiectatic Cyst of the Adrenal

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A review of the literature shows cysts of the adrenal gland to be rare. From 1933 to 1958 only two authentic cysts of the adrenal cortex were recorded in 1100 autopsies performed at Wayne County General Hospital, Eloise, Michigan.[1] According to Hodges and Ellis[1] these tumors are classified as follows:

A. True cysts
   1. Glandular cyst
   2. Lymphangioma
   3. Hemangioma

B. Pseudocysts resulting from:
   1. Hemorrhage
   2. Necrosis and cystic degeneration of a benign or malignant primary tumor
   3. Parasitic infection

A study of 1617 patients[2] suffering from ecchinococcus infection revealed the adrenal gland to be involved in less than 0.5 per cent of cases.

## CASE SUMMARY

A 2 week old white male infant died of pneumonia and purulent parotitis in spite of antibiotic therapy. There had been no evidence of endocrine disturbance during life.

At autopsy the parotid glands did not appear remarkable on gross examination, and microscopically revealed only rare foci containing a few acute inflammatory cells and lymphocytes. There was both gross and microscopic evidence of a bronchopneumonia of the right lung.

The right adrenal gland weighed 3 Gm.; the only significant finding was a small amount of blood in the medullary region. The left adrenal gland weighed 6 Gm. (normal 2½–3 Gm.) and measured 4.0 x 2.5 x 2.0 cm. A thin walled cyst measuring 2.0 cm. in diameter occupied the medullary portion of the gland, and was filled with pink fluid (figs. 1 and 2). The wall of the cyst was made up of connective tissue fibers in which were found a small number of monocytes, reticulum cells, and lymphocytes. The cyst was lined with flattened endothelial cells to which were attached small clusters of lymphocytes.

## DISCUSSION

In our opinion, this cyst, in the absence of hemorrhage, degeneration, or evidence of endocrinopathy, can be best classified as a lymphangiectatic cyst.

Rabson and Zimmerman[3] suggested that the cystic lymphangioma of

* Resident, Children's Hospital.


FIG. 1. Left adrenal gland, external surface

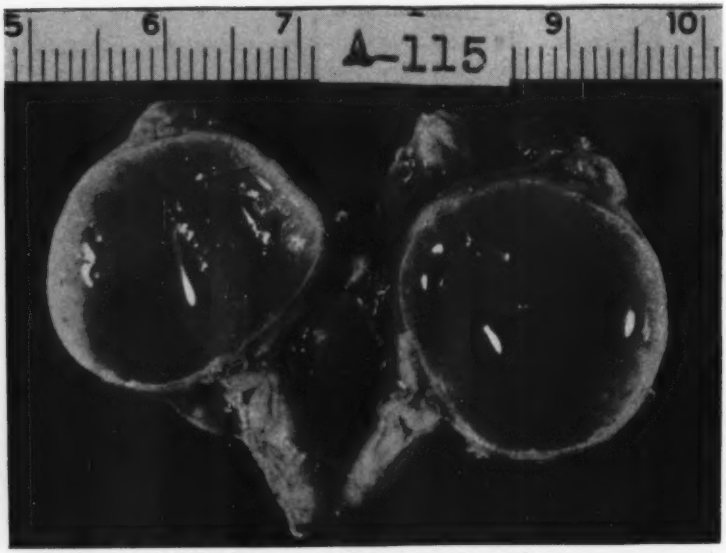


FIG. 2. Left adrenal gland, sagittal section

the adrenal gland should be classified as lymphangiectasis. They concluded that lymphangioma and hemangioma in the adrenal gland are rare, and hematomas are the most common cystic lesions seen. Degeneration of a hematoma also could result in a pseudocyst.

The adrenal cyst is usually discovered at autopsy or surgical exploration in the absence of clinical symptoms. In those cases reported by Rabson and Zimmerman[3], and Reimann and Guyton[4] the adrenal cysts were found at autopsy. Ballance[5] reported a case in which the adrenal cyst was palpable on physical examination. In lymphangiectatic cysts, the contained fluid may be milky or clear, and is surrounded by a smooth thin wall.

A few cases of adrenal cysts accompanied by adrenal insufficiency have been reported in infants. Campbell[6] reported seven children under five years of age with adrenal cysts. None of these children had any clinical evidence of endocrinopathy.

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# Book Review

*Mental Subnormality: Biological, Psychological and Cultural Factors.* A survey of research sponsored by the National Association for Retarded Children. Masland, R. L., Sarason, S. B., and Gladwin, T., New York, Basic Books, 1958, 442 pp.

In their introduction to this book, the authors estimate that, "Of 4,200,000 children born annually in the United States, 3 per cent (126,000) will never achieve the intellect of a 12 year old, 0.3 per cent (12,600) will remain below the 7 year intellectual level, and 0.1 per cent (4,200), if they survive, will spend their lives as completely helpless imbeciles unable to care for

their own creative needs." It was with this background that the National Association for Retarded Children decided to sponsor a program of research aimed at discovering the causes, management and eventually the prevention of mental subnormality. This book is a direct outgrowth of the project and attempts to survey current, projected and needed research in a large and complicated field.

The book is divided into two sections: Part I. The Prevention of Mental Subnormality, is written by Dr. Richard Masland who is the Assistant Director of the National Institutes of Neurological Disease and Blindness, and Part II, Psychological and Cultural Problems in Mental Subnormality by Dr. Seymour B. Sarason, who is Professor of Psychology at Yale University, and Dr. Thomas Gladwin, who is Social Science Consultant with the Community Services Branch of the National Institute of Mental Health. For those readers who do not care to invest in the book itself, both sections have appeared in print previously.*

The authors prefer to use the recommended World Health Organization distinction between mental deficiency—a disability attributable primarily to a demonstrable defect of brain structure or chemistry, and mental retardation—a malfunction due to learning deficiencies arising from unfavorable environmental influences. Both are collectively termed mental subnormality, although Dr. Masland uses the three terms interchangeably. The authors agree that the distinction between retardation and deficiency is frequently difficult to make since it would be a rare "retarded" child in whom one could say there was no organic factor operating and, conversely, a rare "defective" child in whom complicating psychological and environmental factors are not present.

This book fills a real need, since previous books on the subject are sadly out of date and too concerned with classification and description. "Mental Subnormality," on the contrary, asks many more questions than it answers and should provide a much needed stimulus to further research in the field.

Dr. Masland's portion is very tightly written, so much so that one welcomes the short summary he has provided at the beginning; without it, this section is heavy going. He documents very succinctly what is currently known of the pathology, genetics, and epidemiology of mental deficiency, as well as theories of etiology and pathogenesis of prenatal, perinatal, and postnatal causes; he concludes with a short section on

* Masland, R. L.: The prevention of mental retardation; survey of research, A.M.A. J. Dis. Child. **95**(1), Part 2: 3, 1958 and Am. J. Ment. Defic. **62**: 989, 1958.

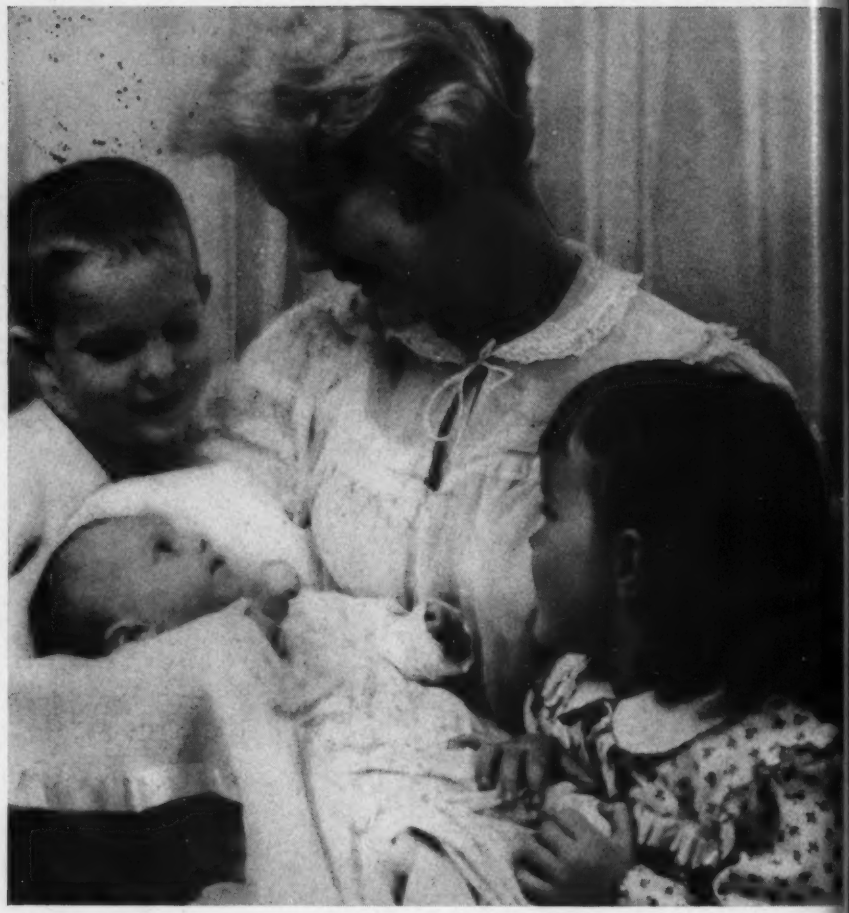
Sarason, S. B., and Gladwin, T.: Psychological and cultural problems in mental subnormality: a review of research. Genet. Psychol. Monogr. **57**: 3, 1958 and Am. J. Ment. Defic. **62**: 1113, 1958.

regeneration of the central nervous system. Dr. Masland has provided a wealth of up-to-date information, not all of which is capable of being assimilated at one reading.

On the other hand, Drs. Sarason and Gladwin's portion, which accounts for about two thirds of the book, is much more loosely written and tends toward verbosity and repetition. Whole sections from preceding articles are quoted verbatim, and one can not help but feel that this section could have been reduced by one-third with little detriment to the book. However, if the reader will persevere, he will find there is much fascinating material presented. The authors emphasize that the problem of mental retardation is social and cultural as well as biological and psychological. They pose some interesting questions: How may social and cultural factors have an interfering effect on the level and quality of the functioning of the mentally retarded? What constitutes intellect and how are our current concepts affected by the types of psychological tests we administer? How narrow a range of functions do the tests currently in use measure? What are the differences in problem-solving ability in performances of individuals in test situations when compared to nontest situations? How do personality factors influence the level of intellectual functioning? The comment that the abnormal behavior of a subnormal child is often "explained" by his low IQ is all too true. The problem of what role early individual variations in sensory reactivity and temperament and their interactions with different types of parental personality, family setting, and social class play in the development of the intellectually normal *or* subnormal child has really not been explored in any systematic manner. There is much more material, equally interesting and provocative.

The authors join in a plea that future training centers for the mentally retarded be set up with reference to the availability of university medical centers, that these centers include diagnostic facilities for the retarded, that responsibility for care of the retarded rest on young physicians with joint staff appointments, and that training programs in mental retardation be set up for physicians at the postgraduate level. The presumption that "nothing can be done," for these subnormal children should be relegated once and for all to the dust-heap where so many of our other long-cherished maxims have landed in the forward march of modern scientific medicine.

J. WILLIAM OBERMAN, M.D.



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